present in the body of the individual. Routes of administration include, but are not limited to, intramuscular, intraperitoneal, intradermal, subcutaneous, intravenous, intraarterially, intraoccularly and oral as well as transdermally or by inhalation or suppository. Preferred routes of administration include intramuscular, intraperitoneal, intradermal and subcutaneous injection.

The pharmaceutical or vaccine compositions according to the present invention comprise about 1 nanogram to about 2000 micrograms of DNA. In some preferred embodiments, pharmaceutical or vaccine compositions according to the present invention comprise about 5 nanogram to about 1000 micrograms of DNA. In some preferred embodiments, the pharmaceutical or vaccine compositions contain about 10 nanograms to about 800 micrograms of DNA. In some preferred embodiments, the pharmaceutical or vaccine compositions contain about 0.1 to about 500 micrograms of DNA. In some preferred embodiments, the pharmaceutical or vaccine compositions contain about 1 to about 350 micrograms of DNA. In some preferred embodiments, the pharmaceutical or vaccine compositions contain about 25 to about 250 micrograms of DNA. In some preferred embodiments, the pharmaceutical or vaccine compositions contain about 100 to about 200 micrograms DNA.

The pharmaceutical or vaccine compositions according to the present invention are formulated according to the mode of administration to be used. In cases where pharmaceutical or vaccine compositions are injectable pharmaceutical compositions, they are sterile, pyrogen free and particulate free. An isotonic formulation is preferably used. Generally, additives for isotonicity can include sodium chloride, dextrose, mannitol, sorbitol and lactose. In some cases, isotonic solutions such as phosphate buffered saline are preferred. Stabilizers include gelatin and albumin. In some embodiments, a vasoconstriction agent is added to the formulation.

In some embodiments, nucleic acid molecules are delivered to the cells in conjunction with administration of a polynucleotide function enhancer or a "genetic vaccine facilitator" (GVF) agent. Polynucleotide function enhancers are described in U.S. Patent No. 5,593,972, U.S. Patent No. 5,981,505, and International Application Serial Number PCT/US94/00899, filed January 26, 1994, which are each incorporated herein by reference. GVF agents are described in U.S. Patent No. 5,739,118, U.S. Patent No. 5,837,533, and International Application Serial Number PCT/US99/04332, international filing date February 26, 1999, each of which is incorporated herein by reference.

The co-agents, which are administered in conjunction with nucleic acid molecules, may be administered as a mixture with the nucleic acid molecule, or may be administered separately,

simultaneously, before, or after administration of the nucleic acid molecules. In addition, other agents which may function as transfecting agents and/or replicating agents and/or inflammatory agents, and which may be co-administered with or without a GVF, include growth factors, cytokines, and lymphokines, such as α-interferon, γ-interferon, platelet derived growth factor (PDGF), tumor necrosis factor (TNF), epidermal growth factor (EGF), interleukin-1 (IL-1), IL-2, IL-4, IL-6, IL-8, IL-10, and IL-12, as well as fibroblast growth factor, surface active agents, such as immune-stimulating complexes (ISCOMS), Freund's incomplete adjuvant, lipopolysaccharide (LPS) analogs, including monophosphoryl Lipid A (MPL), muramyl peptides, quinone analogs, vesicles, squalene, and squalene and hyaluronic acid. In some embodiments, an immunomodulating protein may be used as a GVF.

Nucleic acid molecules which are delivered to cells according to the invention may serve as genetic templates for proteins that function as prophylactic and/or therapeutic immunizing agents. In preferred embodiments, the nucleic acid the nucleic acid molecules comprise the necessary regulatory sequences for transcription and translation of the coding region in the cells of the animal.

The present invention relates to improved attenuated live vaccines and improved vaccines which use recombinant vectors to deliver foreign genes that encode antigens. Examples of attenuated live vaccines and those using recombinant vectors to deliver foreign antigens are described in U.S. Patent Nos.: 4,722,848; 5,017,487; 5,077,044; 5,110,587; 5,112,749; 5,174,993; 5,223,424; 5,225,336; 5,240,703; 5,242,829; 5,294,441; 5,294,548; 5,310,668; 5,387,744; 5,389,368; 5,424,065; 5,451,499; 5,453,364; 5,462,734; 5,470,734; and 5,482,713, each of which is incorporated herein by reference. Gene constructs are provided which include the nucleotide sequence that encodes the capsid protein is operably linked to regulatory sequences that can function in the vaccinee to effect expression. The gene constructs are incorporated in the attenuated live vaccines and recombinant vaccines to produce vaccines according to the invention.

The pharmaceutical and vaccine compositions according to this aspect of the present invention comprise about 0.1 μg to about 1000 μg of DNA. In some preferred embodiments, the pharmaceutical and vaccine compositions contain about 1 μg to about 500 μg of DNA. In some preferred embodiments, the pharmaceutical and vaccine compositions contain about 25 μg to about 250 μg of DNA. Most preferably, the pharmaceutical and vaccine compositions contain about 100 μg DNA.

The pharmaceutical and vaccine compositions according to this aspect of the present invention are formulated according to the mode of administration to be used, as discussed above. One having ordinary skill in the art can readily formulate a nucleic acid molecule that encodes WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or a functional fragment thereof. In cases where intramuscular injection is the chosen mode of administration, an isotonic formulation is used. Generally, additives for isotonicity can include sodium chloride, dextrose, mannitol, sorbitol and lactose. Isotonic solutions such as phosphate buffered saline may be used. Stabilizers include gelatin and albumin. In vaccine compositions, the addition of adjuvants or immunostimulating agents may be desirable.

Apoptosis assay

Another aspect of the present invention relates to a method of identifying compounds which inhibit the WNV Cp or capsid or other protein of other viruses including *Flavivirus* or *Pestivirus*, or a functional fragment thereof, from inducing cells to undergo apoptosis which comprises the steps of first contacting, in the presence of a test compound, said cells with an amount of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid or other protein, or a functional fragment thereof, sufficient to induce a detectable level of apoptosis, and then observing said cells to determine if apoptosis occurs in the presence of the test compound. Compounds which interfere with the apoptosis-inducing activity of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid or other protein, or functional fragments thereof, may be useful as drugs for combating the virus and treating WNV and other virus infections including *Flavivirus* or *Pestivirus* infections.

According to this aspect of the invention, compounds are identified which inhibit the ability of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or functional fragments thereof, to induce apoptosis in hyperproliferating cells. An assay is provided which compares apoptosis induction by WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or functional fragment thereof, in the presence or absence of test compounds. Using this assay, compounds can be identified that inhibit the apoptosis-inducing activity of WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or functional fragments thereof. Such compounds may be useful as anti-WNV and/or anti-*Flavivirus* or anti-*Pestivirus* therapeutics.

The method of the present invention comprises the step of contacting cells with WNV or other viruses including *Flavivirus* or *Pestivirus* capsid protein, or functional fragment thereof,